

the diagnosis of which rested solely upon the morphological and staining characteristics of the organisms found; that is to say, upon the fact that a Gram-negative, intracellular, biscuit-shaped diplococcus was found. If the term gonorrheal or gonococcus vaginitis were for the present dropped from the literature and the term epidemic vaginitis substituted (this name not suggesting to the lay mind a venereal disease), I think it would be much easier to handle these cases from a public health stand-point.

It appears to me very evident that until we are in a position to make vaginitis a reportable disease and enforce the ordinary health regulations which are used in other reportable diseases we are not justified in excluding these cases from our public schools.

#### HOW CLOSELY DO THE WASSERMANN REACTION AND THE PLACENTAL HISTOLOGY AGREE IN THE DIAGNOSIS OF SYPHILIS?

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THE unimpeachable diagnosis of syphilis is made upon the demonstration of the *Spirocheta pallida*. After this fact became established the hope was entertained that the organism might be found regularly in syphilitic placenta, but competent investigators declare that although prolonged search (Trinchesi<sup>1</sup>) is more frequently successful, the spirochetes are readily demonstrable in the placenta approximately in every third case of syphilis (Mohn,<sup>2</sup> Bab,<sup>3</sup> Graefenberg<sup>4</sup>). Generally, therefore, the diagnosis rests upon the less specific evidence of the histological changes in the chorionic villi or the Wassermann reaction in the mother's blood. As neither of these tests affords absolute proof regarding the presence of syphilis, we should know how frequently they point to the same conclusion; and, if not always, is one test more reliable than the other?

Besides variations in the Wassermann reaction due to the technic

<sup>1</sup> Bakteriologische und histologische Untersuchungen bei kongenitaler Lues, München. med. Wchnschr., 1910, lvii, 570.

<sup>2</sup> Die Veränderungen an Placenta, Nabelschnur, und Eihäuten bei Syphilis und ihre Beziehungen zur *Spirochete pallida*, Ztschr. f. Geburtsh. u. Gynäk., 1907, lix, 263.

<sup>3</sup> Bakteriologie und Biologie der kongenitalen Syphilis, Ztschr. f. Geburtsh. u. Gynäk., 1907, lx, 161.

<sup>4</sup> Der Einfluss der Syphilis auf die Nachkommenschaft, Arch. f. Gynäk., 1909, lxxvii, 190.

employed<sup>5</sup> and to the interpretation of the degree of fixation, the specificity of the test is impaired, since occasionally a positive reaction is independent of syphilis. Thus, fixation has been observed in cases of malaria, of malignant growth, of hepatic disease, and of some tropical infections, as sleeping sickness. On the other hand, in an appreciable number of syphilitics, the reaction is negative even during the secondary period of the disease. If interpreted in the light of the clinical history the reaction is rarely misleading, but this means, of course, that as yet implicit reliance upon the test is not justified. With newborn infants, Bar and Daunay<sup>6</sup> report notable inconsistency in the Wassermann; frequently they obtained a negative reaction when syphilis was known to exist.

It is also true that, one after another, the placental phenomena regarded as characteristic of syphilis have been questioned. Upon the gross appearance of the organ it is unsafe to base a diagnosis, for macroscopic signs of the disease are not constant; they were absent in 82 of 160 syphilitic placenta which Mracek<sup>7</sup> examined. And, conversely, when the fetus dies sometime before it is born, whether syphilis is the cause or not, the placenta may be firmer than usual, its color may be a pale gray, and the maternal surface may have a greasy appearance.

Large placenta do not, as was once supposed, necessarily denote syphilis. Labourdette<sup>8</sup> found that the relationship between the weight of the placenta and the weight of the fetus may not be used to establish a diagnosis. In cases in which syphilis was excluded, not infrequently this ratio was 1 : 5, 1 : 4, and occasionally 1 : 3. When the infant is premature this ratio is more significant, but prior to term we must remember that the placenta normally weighs more than a sixth of the weight of the fetus.

In the umbilical cord, as in the placenta, Emmons<sup>9</sup> had great difficulty in demonstrating spirochetes, and no syphilitic cord lesion is regularly found. An exudative inflammation about the vessels which Bondi<sup>10</sup> declared pathognomonic for syphilis may be caused by bacterial infection.<sup>11</sup> In typical cases when due to syphilis the infiltration appears at the fetal end; when due to placental bacteremia, at the maternal end of the cord. However, exceptions are frequent and greatly impair the diagnostic value of this lesion.

<sup>5</sup> Swift: Serum Diagnosis of Syphilis, Jour. Am. Med. Assn., 1916, lxxvi, 599.

<sup>6</sup> Recherches sur le sero-diagnostic de la Syphilis chez la femme enceinte et l'enfant nouveau-ne (Methode de Wassermann), Obstetrique, 1909, n. s., ii, 192.

<sup>7</sup> Die Syphilis der Mutter und der Neugeborenen, Wien. klin. Wchnschr., 1903, xvi, 519.

<sup>8</sup> Gros Placentas et Syphilis, Paris Thesis, 1915.

<sup>9</sup> The Diagnostic Value of the Search for Spirocheta Pallida in the Umbilical Cord of the Newborn, Boston Med. and Surg. Jour., 1910, clxii, 640.

<sup>10</sup> Die Syphilitischen Veränderungen der Nabelschnur, Arch. f. Gynäk., 1903, lxi, 223.

<sup>11</sup> Slemons: Placental Bacteremia, Jour. Am. Med. Assn., 1915, lxxv, 1265.

The most trustworthy evidences of placental syphilis to which Fraenkel<sup>12</sup> directed attention in 1873 are the histological changes in the chorionic villi. When freshly teased in dilute hydrochloric acid, originally recommended by Eckhardt,<sup>13</sup> or in water and examined under the microscope, the syphilitic villi appear abnormally large, opaque, and irregular in shape, with swollen ends. Characteristically the branching is limited and the bloodvessels are indistinct. While these findings are suspicious before the diagnosis of syphilis is made, stained sections should be examined. These provide a more satisfactory opportunity for studying the lesion.

The pathological process begins as a proliferative inflammation in the walls of the smallest bloodvessels—those of the terminal villi. Frequently the lumen of the vessel is obliterated. The enlargement of the villi is the result of the proliferation of the stroma. At last the syncytium which covers the villi proliferates and invades the underlying tissue.

While the changes in the villi constitute the most distinctive evidence of placental syphilis they have not been accepted by everyone as pathognomonic. In 1903 Hitschmann and Volk<sup>14</sup> observed a similar microscopic picture in cases in which a history of syphilis was unobtainable. "All the histological evidence thus far counted characteristic of placental syphilis," they dramatically conclude, "may be found in other conditions and even in normal cases. Perhaps these are cases of occult syphilis; who will bring the proof?" Since this question was asked the serological method of establishing the diagnosis has been devised; and we have accepted the opportunity to control the microscopic examination of the placenta with the Wassermann reaction in the mother's blood.

Two series of observations have been made, namely, the first upon 260 consecutive cases,<sup>15</sup> in San Francisco, in which the Wassermann reaction was made by Dr. L. S. Schmitt,<sup>16</sup> and the second upon 100 consecutive cases in New Haven, where Dr. A. L. O'Shansky<sup>17</sup> made the serological tests. These observations may be classified as follows:

Group.	Wassermann.	Placenta.	Number of cases.			
I	Negative	Negative	243 (San Francisco)	93 (New Haven)		
II	Positive	Positive	7 "	3 "	"	"
III	Negative	Positive	1 "	0 "	"	"
IV	Positive	Negative	10 "	4 "	"	"

<sup>12</sup> Ueber Placentarsyphilis, *Arch. f. Gynäk.*, 1873, v. 1.

<sup>13</sup> Quoted by Rosinski: *Die Syphilis in der Schwangerschaft*, Stuttgart, 1903.

<sup>14</sup> *Zur Frage der Placentarsyphilis*, *Wien. klin. Wchnschr.*, 1903, xvi, 822.

<sup>15</sup> Slemons: The Results of Routine Study of the Placenta, *Am. Jour. Obst.*, 1916, lxxiv, 177.

<sup>16</sup> Both Doctor Schmitt and Doctor O'Shansky used two antigens, namely, (1) acetone insoluble alcoholic extract of ox heart, and (2) cholesterinized alcoholic extract of ox heart.

<sup>17</sup> *Loc. cit.*

In Groups I and II, which include 345 cases (95 per cent.), the Wassermann reaction and the placental histology agree absolutely and indicate the presence of syphilis in 10 cases, its absence in 235 cases.

The single case in Group III, in spite of the negative Wassermann, must be regarded as syphilitic. This woman, aged twenty-seven years, had four consecutive miscarriages. The pregnancy we observed ended spontaneously at the eighth lunar month. The fetus, 40 cm. long, weighed 1960 grams. The placenta weighed 480 grams (one-quarter the weight of the fetus) and the chorionic villi were definitely syphilitic. At autopsy upon the fetus the lesions of congenital syphilis were demonstrable. Therefore the weight of evidence points to the presence of syphilis, and we conclude that occasionally when the Wassermann reaction is negative the placental findings are more reliable.

Other investigators have found a negative Wassermann reaction in cases of syphilis. In the secondary period of the disease the test was positive in 87 per cent. of Bruch's<sup>18</sup> cases, 92 per cent. of Levaditi's, 96 per cent. of Blumenthal's, 98 per cent. of Blaschko's and 100 per cent. of Schmenfeld's. Later in the disease Kirschman<sup>19</sup> obtained a positive reaction in only 68 of 100 syphilitic patients. When the infant was syphilitic, Knopfmacher and Lehdorff<sup>20</sup> failed to obtain a positive Wassermann in the mother's blood in 9 per cent. of his cases. If experience counts, these observations made several years ago are less accurate than serologists now obtain. At present many authorities hold that active syphilis is always accompanied by a positive Wassermann, though with latent syphilis they concede the frequency of a negative reaction approximates 20 per cent. (Kolmer<sup>21</sup>).

Group IV, comprising 14 cases (10 in San Francisco and 4 in New Haven), is not so discordant as would at first appear, for strong fixation (+ + +) occurred in only two instances. One of these patients was suffering from a streptococcus infection which probably was responsible for the positive reaction; at least the Wassermann test alone raised the question of syphilis. There was no history of a specific infection, and the chorionic villi were normal. On the other hand the fetal surface of the placenta was the seat of an inflammatory infiltration; streptococci were found in the subamniotic connective tissue and also in microscopic sections of the cord. On the third day of the puerperium the organism was isolated from the uterine cavity. The infant died of hemophilia; at autopsy none of the lesions of congenital syphilis were

<sup>18</sup> Bruch, Levaditi, Blumenthal, Blaschko, Schmenfeld, Kirschmann: Quoted by Labourdette (8).

<sup>19</sup> Loc. cit.

<sup>20</sup> Das Collesche Gesetz und die neuen Syphilis-forschungen, Jahrb. f. Kinderh., 1910, lxxi, 156.

<sup>21</sup> Syphilis and Life Insurance, Jour. Am. Med. Assn., 1916, lxxi, 1435.

demonstrable. Therefore the positive Wassermann would not seem attributable to syphilis.

Another case in this group with a strongly positive Wassermann reaction, but negative placental findings was syphilitic. On September 5 and again on the time of delivery, November 18, 1914, the serological test was positive. Furthermore, the mother gave a history of specific infection eight months previously and had not been treated. On account of the maceration of the fetus the autopsy findings were not helpful.

The teased chorionic villi were suspicious of syphilis, though the stained sections were negative. However, other areas of the placenta might have presented the characteristic evidence of syphilis, for normal areas may occur in syphilitic placentae. Clearly in this case the weight of evidence favors the diagnosis of syphilis and indicates that occasionally the Wassermann reaction is more trustworthy than the placental histology—a situation which will exist most frequently in cases of postconceptional syphilis.

The remaining 12 cases of Group IV presented faintly a positive Wassermann reaction. The serologist reported 8 results as a single + (25 per cent. fixation) and 4 results as a double ++ (50 per cent. fixation). It is significant that 10 of these patients were suffering from eclampsia or a toxemia of pregnancy with albuminuria.

In the early history of the Wassermann test the occurrence of a suggestive or a positive reaction in cases of eclampsia was noted by Bunzel,<sup>22</sup> Daunay,<sup>23</sup> and others. Semon<sup>24</sup> obtained 3 positive, 9 negative, and 1 doubtful reaction in eclamptics without syphilis. We are unable to substantiate Semon's statement that the reaction is negative when the auto-intoxication is mild. On the contrary the severity of the intoxication bears no relation to the degree of fixation. A double + was twice reported when the albuminuria was of a mild type, while in several eclamptics with severe albuminuria we obtained a single +.

It is almost certain in these cases that the fixation was due to the metabolic disturbance. In similar circumstances Bunzel observed that the Wassermann became negative as the toxic symptoms disappeared. We have not been able to make repeated observations upon our patients, but their histories excluded syphilis and the placenta were normal. The infants were healthy at birth, in excellent condition when they left the hospital, and when visited four weeks later none of them had developed stigmata of congenital syphilis.

The frequency with which a positive Wassermann reaction

<sup>22</sup> Untersuchungen auf Komplementinde Substanzen im Blute von Schwangeren und Wöchnerinnen, *Zentralbl. f. Gynäk.*, 1909, xxx, 975.

<sup>23</sup> Quoted by Davis: Syphilis in its Relation to Obstetrics, *Tr. Am. Gynec. Soc.*, 1916.

<sup>24</sup> Eklampsie und Wassermann Reaktion, *Zentralbl. f. Gynäk.*, 1911, xxxv, 556.

occurs during toxemia of pregnancy and the question of its association with a definite form of auto-intoxication are pertinent problems. The limited data at hand will not permit an uncompromising view, but in our experience every third or fourth case of threatened and active eclampsia presents some degree of fixation, generally between 25 and 50 per cent. Whether syphilis underlies the toxemia is a question which can scarcely be raised, since Bunzel demonstrated that the serological reaction becomes negative as the auto-intoxication of pregnancy disappears.

In the course of chemical analysis of the blood having found that the cholesterol varies during pregnancy, and that the amount of this substance, while normal in some cases of toxemia, is greatly increased in others, we suspected that the latter group might be the one in which the faintly positive Wassermann reaction occurred. But this is not true. A negative Wassermann was reported for patients when the cholesterol amounted to 245, 180, and 125 mg. per 100 c.c., whereas 25 per cent. fixation was noted when the cholesterol was 144 mg.

In cases in which none of the classical symptoms of toxemia are present and the pregnancy apparently is normal, occasionally the Wassermann in the mother's blood is faintly positive. We encountered only two such cases, but Pedrini<sup>25</sup> observed the phenomenon more frequently, and in consequence records a positive Wassermann in 10.7 per cent. of the pregnant women he examined. Generally the reaction is faint, and without clinical evidence of syphilis it would be interpreted as negative. For the present the meaning of fixation in these circumstances is unknown, but probably it is explained by the presence of some substance in the blood referable to the metabolism of pregnancy. At all events the occurrence of the phenomenon in normal cases as well as toxemias emphasizes the value of controlling the diagnosis of syphilis with the microscopic study of the chorionic villi.

To recapitulate, the comparative study of the Wassermann reaction and the placental findings in 360 consecutive confinements indicates that the tests agree absolutely in 95 per cent. of obstetrical patients.

The chief source of confusion lies in the presence of a toxemia of pregnancy, which may be responsible for a faintly positive reaction. In these circumstances the fixation should not be taken to indicate syphilis, and accepting that interpretation, the serological test and the placental agree 99 times out of a 100.

Frankly contradictory results were encountered in three instances. One patient who gave a positive Wassermann was not syphilitic. The other two patients were syphilitic; the first presented a negative

<sup>25</sup> Una casistica di sieroreazioni di Wassermann nel campo ostetrico, *Ann. di Ostet.*, 1910, II, 363.

Wassermann but positive placenta, the second a positive Wassermann but negative placenta. Therefore it is impossible to say that one test is more reliable than the other, except in cases of postconceptional syphilis, and then the Wassermann reaction is more trustworthy. On the other hand, in latent syphilis the placental histology alone may confirm what is learned from the maternal history or the examination of the fetus.

At present the advisable procedure for the recognition of syphilis in parturient women begins with the study of the freshly teased chorionic villi—an examination which should be made routinely in obstetrical practice. If their appearance points toward the presence of syphilis, hardened and stained sections of the placenta must be studied and the Wassermann reaction in the mother's blood must be determined. Furthermore, all these observations should be made whenever the fetus is premature, macerated, or stillborn.

Instances in which the Wassermann reaction and the placental histology yield contradictory results are rare: If these cases are judged in the light of subsequent serological tests upon the mother, of facts in her history, and of the results of clinical or pathological examination of the fetus, they may be properly classified.

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### A STUDY OF VON JAKSCH'S ANEMIA.\*

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ALTHOUGH cases of anemia accompanied by enlargement of the spleen and occurring in children were described clinically by Gretscl<sup>1</sup> as long ago as 1866, and pathologically by Cohnheim<sup>2</sup> in the preceding year, it was not until more than twenty years later, when the examination of the blood began to play a prominent part in clinical investigations, that the various conditions included under this head began to be separated one from the other. In 1889 von Jaksch<sup>3</sup> described a case of leukemia in a child, aged fourteen months, and in the following year<sup>4</sup> he reported 3 cases of enlarged spleen in children, a condition which he called anemia pseudoleukemica infantum. This was characterized by a diminution in the hemoglobin and in the number of red cells, marked persistent leukocytosis, sometimes glandular enlargement, slight enlargement of

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